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Effects of dopaminergic medication on reward and punishment sensitivity in risky decision-making

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Dopaminergic drug effects on risky decision-making

Abstract

Pathological gambling (PG) is a behavioural addiction similar in many aspects to substance use disorder (Clark & Limbrick-Oldfield, 2014). PG involves excessive risk taking and (monetary) reward. Neurotransmitter dopamine is of interest in relation to risk taking and PG due to its central role in learning from reward and punishment (Cools et al., 2009). Moreover, some Parkinson's disease patients develop PG following dopamine replacement therapy (Clark & Dagher, 2014). The aim of this study was to examine the effects of dopaminergic modulation on risk-taking behaviour in healthy and PG individuals. Dopamine D_2/D_3 receptor antagonist sulpiride and a placebo drug were administered in order to transiently alter dopamine transmission during an economic decision-making task. Participants chose between sure choices of winning (or losing) a certain amount of money and gambles with different probabilities to win (or lose) money. A prospect theory (Kahneman & Tversky, 1979) modelling approach was used to estimate parameters reflecting sensitivity to outcomes and probabilities and optimism about risk, based on the varying amounts of money and probabilities in the task. We found that sulpiride decreased distortion in weighting the probabilities of potential gains. That is, participants overweighted low and underweighted moderate to high winning probabilities less under sulpiride compared with placebo. However, the drug effect did not differ between the groups and was not found in the loss domain. In conclusion, we found evidence for a relationship between dopamine and risky decision-making in the distortion of probability weighting.

Keywords: risky decision-making, dopamine, pathological gambling, reward, punishment

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1. Introduction

Risk is a pervasive aspect of our everyday lives. We have to make risky decisions such as whether to run to the bus despite a red traffic light, whether to take insurance, or whether to change jobs. Importantly, we do not know the outcome of these choices beforehand and, therefore, have to make a trade-off between the likelihood of each possible outcome and its (negative or positive) subjective value. Decision-making under risk refers to situations where we know the likelihood of different outcomes. In economics, this is distinguished from decision-making under uncertainty where this likelihood is unknown. Behavioural economists have come up with theoretical models of risky-decision making that allow quantifying risk behaviour, and thus, studying both general tendencies and individual differences in human populations. In particular, the framework of *prospect theory* makes it possible to parse decision-making behaviour into different components. In some cases, such as in gambling, risk-taking can become excessive and detrimental to social, financial or physical well-being. In this project, we were interested in studying how risk-taking behaviour is modulated by dopamine, a neurotransmitter that has been associated with reward (gain) and punishment (loss) processing, in both healthy participants and individuals suffering from gambling addiction.

1.1. Prospect theory

Prospect theory (Kahneman & Tversky, 1979; Tversky & Kahneman, 1992) is a behavioural economics theory that that was developed in response to empirical evidence that, in many ways, human agents do not act as rational decision-makers in the economical sense. For example, humans tend to be averse to options involving risk, in comparison to situations with sure gains. In more specific terms, humans do not always choose an option with the highest expected value, that is, the value of the outcome times its probability. For example, people tend to choose €45 for sure over a 50% chance of winning €100 or else nothing.

Prospect theory posits that this departure from rational economic decision-making can result from the fact that human agents do not perceive increases or decreases in the value of the outcome in a linear fashion. Therefore, the initial intuition of a decision-maker attempting to maximize expected value can be replaced with the maximization of expected *utility*, referring to the decision maker's subjective sensitivity to the value of the outcome. Referring to the earlier example, the expected utility of €45 for sure is higher than the expected utility of €50 in the risky option (Fig. 1). The objective outcome value of the sure option, €45, is almost half of €100. However, due to the non-linear valuation of outcomes, the subjective utility of €45 (notated as U(€45)) is more than almost half of the utility of €100 (shown as 0.5 x U(€100) in Figure 1), thus making the sure option of €45 preferred in most cases. The behavioural observation of diminishing sensitivity to outcome value is modelled in the value function of prospect theory (Fig. 2A). Typically, the relationship between objective outcomes and their subjective values ($U(x)$) is concave for gains and convex for losses. Concave (convex) function is associated with risk averse (seeking) behaviour both in the gain and loss domains. The value function is often parameterised as a power function x^{α}, with α controlling the curvature of the function.

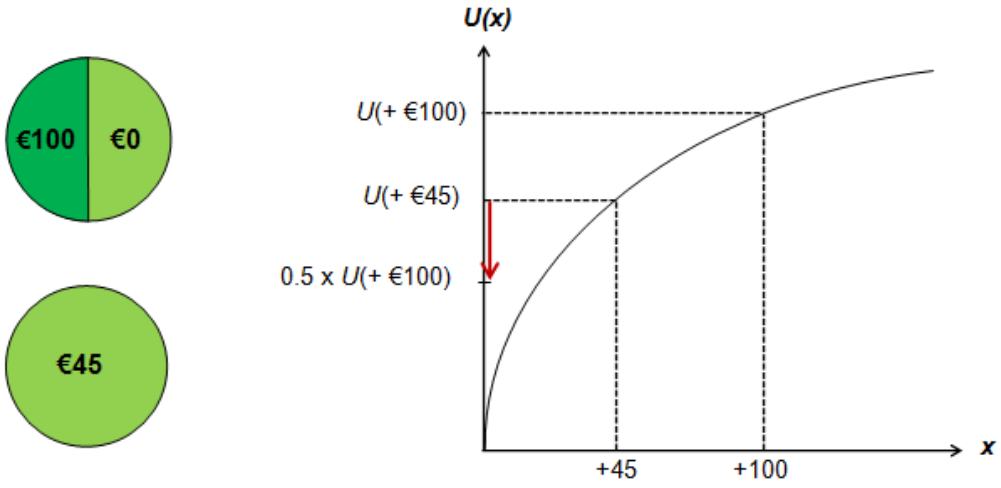

Figure 1. An example of a prospect with its associated utilities *U(x)* over values *x*. The arrow illustrates how the expected utility of €50 in the gamble is less than that of €45 in the sure option due to diminishing sensitivity to gain outcomes.

Another observation of Kahneman and Tversky in contrast to earlier economics theories was that, in general, people have different sensitivities to probabilities, with a tendency to overweight low probabilities and underweight moderate to high probabilities. Therefore, in addition to outcomes, human agents also do not perceive probabilities in a linear fashion. This is modelled in the probability weighting function of prospect theory (Fig. 2B). Typically, the function has an inverse S-shape. With more overweighting of low probabilities and underweighting of moderate to high probabilities, the distortion of the function increases and the standard inverse S-shape becomes more exaggerated. Risk aversion is also influenced by global shifts in risk preferences, also called optimism or pessimism about risk, modelled as higher or lower elevation of the probability weighting function. With a change in the elevation of the function, all of the subjective probabilities are shifted in the same direction. The more risk-seeking the behaviour is in the gain domain, the higher the elevation of the function is. In the loss domain, the relationship is opposite, with higher elevation reflecting more risk aversion. The described prospect theory approach can be used to quantify and parse risk-taking behaviour into different components as well as study individual differences in risk-taking behaviour, including comparisons between healthy and pathological groups of individuals.

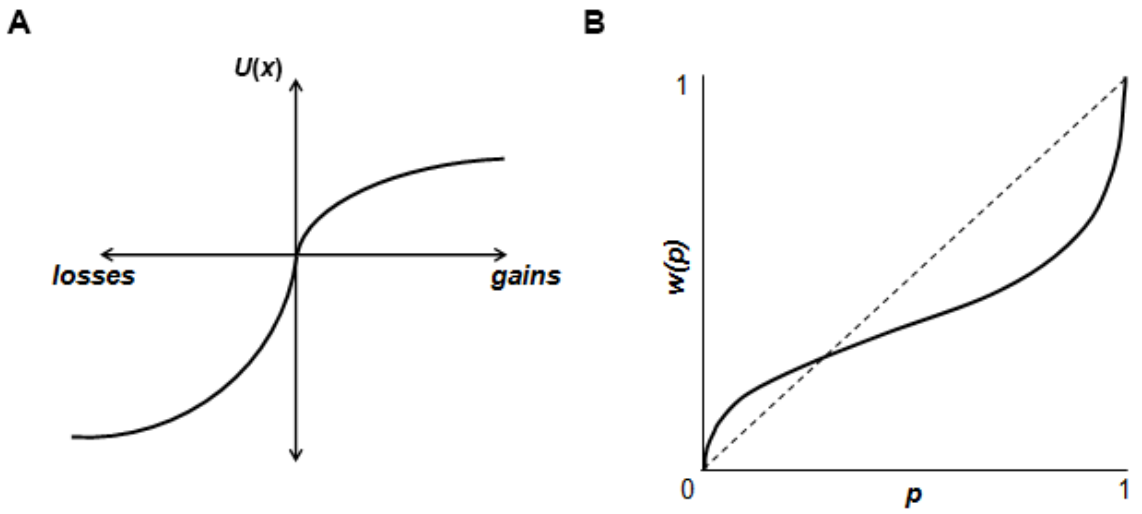

Figure 2. Prospect theory functions, *A.* Value function, *B.* Probability weighting function *w*(*p*) (adapted from Fox & Poldrack, 2008).

1.2. Pathological gambling

Pathological gambling (PG), also called gambling disorder, is a psychiatric disorder characterised by persistent and uncontrolled gambling behaviour despite negative consequences. It is associated with extreme risk-taking with regard to monetary rewards. PG is classified as an addictive disorder in the *DSM-5* (American Psychiatric Association, 2013) and has been found to be similar in many aspects to substance use disorder (SUD). For example, PG and SUD share symptoms, such as craving induced by addiction-related stimuli, continuation of the behaviour despite negative consequences, tolerance, and withdrawal (see Goodman 2008; Grant, Brewer, & Potenza, 2006; Wray & Dickerson, 1981; Castellani & Rugle, 1995). PG is associated with sensation-seeking and impulsivity, personality traits also involved in substance abuse (Zuckerman & Neeb, 1979; Castellani & Rugle, 1995; Slutske, Caspi, Moffitt, & Poulton, 2005). Moreover, PG has been claimed to share similar neurobiological substrates with other addictive disorders, most notably, dysregulation of dopaminergic mesolimbic circuits (see Goodman, 2008; Potenza, 2013).

1.3. Dopamine, gambling, and risk-taking

Specific evidence for the involvement of dopamine in PG comes from studies on Parkinson's disease patients, showing that a subset of patients develop compulsive behaviours, impulsivity, and gambling problems after receiving dopaminergic replacement therapy (Molina et al., 2000; Gallagher, O'Sullivan, Evans, Lees, & Schrag, 2007). Dopamine D_2 receptor agonists are sufficient to cause impulse controls disorders in Parkinson's disease (Gschwandtner, Aston, Renaud, & Fuhr, 2001; Dodd et al., 2005). Moreover, these gambling problems are reduced or disappear entirely when the agonist drug is no longer taken (Gschwandtner et al., 2001; Dodd et al., 2005).

Various animal studies have demonstrated the role of dopamine in risk-taking behaviour and have thus given support to the hypothesis of a common neurobiological basis between substance and behavioural addictions. Low D_2/D_3 receptor expression in the dorsal striatum has been associated with

wager-sensitivity trait in rats (Cocker, Dinelle, Kornelson, Sossi, & Winstanley, 2012), corresponding to risk aversion and preference for the sure option (see Sescousse & den Ouden, 2013). Another study found that amphetamine, triggering large striatal release of dopamine (Laruelle et al., 1995; Drevets et al., 2001), increased preference for risky choice in rats and that the effect was blocked or attenuated when D_1 or D_2 receptor antagonists were administered together with amphetamine (St Onge & Floresco, 2009). Correspondingly, D_1 and D_2 receptor agonists had a similar effect to that of amphetamine, whereas stimulation of D_3 receptors was associated with the opposite effect.

Human positron emission tomography (PET) studies also provide evidence for the involvement of dopamine in risk-taking and pathological gambling. Healthy participants have been shown to have increased mesolimbic dopamine release during gambling tasks (Thut et al., 1997; Zald et al., 2004; Hakyemez, Dagher, Smith, & Zald, 2008). Pathological gamblers seem to have an increased dopamine response to an amphetamine challenge (Boileau et al., 2014) and higher dopamine synthesis capacity (van Holst et al., 2016) compared with healthy controls. The severity of gambling symptoms is associated with mesolimbic dopamine release in PG (Joutsa et al., 2012). On the other hand, no significant group differences have been found between pathological gamblers and healthy controls in D_2/D_3 receptor binding (Boileau et al., 2012; Clark et al., 2012), even though a robust reduction in receptor availability has been demonstrated in SUD (Martinez et al., 2007; Fehr et al., 2008; Volkow et al., 2010). It could be that the reduction in D_2/D_3 receptor availability is a consequence of exposure to the addiction-related substance instead of a common vulnerability marker for all addictions, and therefore, is not found in pathological gambling and other behavioural addictions (see Clark et al., 2013; Groman et al., 2012).

Therefore, there is robust evidence that dopamine, in particular through the stimulation of D_2/D_3 receptors, is involved in modulating risk-taking behaviour. However, the specific mechanisms through which dopamine may act to foster PG remain elusive. In addition, it is unclear which components of risky decision-making are affected by dopamine. Consequently, further studies are needed to establish whether dopamine is involved, for example, in sensitivity to outcomes or biases in probability weighting.

1.4. Earlier research and research questions

Currently, there are only a few studies that have examined pathological gambling from the point of view of prospect theory or investigated the role of dopamine in risk-taking. In the study of Zhong and colleagues (2009), the 9-repeat allele of dopamine transporter (DAT1) gene was associated with more risk-tolerance (i.e., risk-seeking) in the gain domain. This particular allele is also associated with lower dopamine tone, suggesting that lower levels of available (striatal) dopamine are linked to risk-seeking behaviour in the gain domain, where risk aversion is typical. Other studies have found similar associations (Dreber et al., 2009; Kuhnen & Chiao, 2009; Mata, Hau, Papassotiropoulos, & Hertwig, 2012). Takahashi and colleagues (2010) found that striatal dopamine D_1 (but not D_2) receptor binding, as measured by PET, was negatively correlated with the level of probability distortion in healthy participants. In a study by Norbury, Manohar, Rogers and Husain (2013), a D_2/D_3 receptor agonist drug cabergoline increased the influence that probability of winning had on choices. That is, participants chose gambles with high probability of winning compared with those with low probability of winning in a more exaggerated fashion under the influence of the drug, with the effect being strongly dependent on the level of sensation-seeking trait. In a more recent study (Rutledge, Skandali, Dayan, & Dolan, 2015), administration of L-DOPA was associated with an increase in the number of risky choices in the gain but not loss domain. However, the change in behaviour was not ascribed to a change in risk aversion in the prospect theory framework but rather to a Pavlovian approach bias.

Ligneul, Sescousse, Barbalat, Domenech and Dreher (2013) studied healthy controls and pathological gamblers within the prospect theory framework in a decision-making task with sure options and risky gambles. They contrasted two hypotheses, namely, that pathological gamblers distort winning probabilities more than controls or that gamblers overweight the entire range of probabilities compared with controls. These could have a similar effect on risk-taking in the low probability range, corresponding to most gambling games. It was found that gamblers have a general shift in their risk preferences (i.e., they show an optimism bias) and risk-seeking in the gain domain compared with control participants,

which supported the latter hypothesis. Moreover, gambling severity (as measured by South Oaks Gambling Screen, Lesieur & Blume, 1987) was positively correlated with the optimism parameter. The study gave no support to the hypothesis of gamblers having more highly distorted weighting of probabilities than controls. In the current study, a very similar, and in some ways improved, paradigm was used in attempt to replicate the result and to study the effect of dopamine on risk aversion (reflected in the shape of the value function), global attitude on risk, and sensitivity to probabilities. Importantly, this study extends the design to the loss domain.

Based on these earlier results, we were interested in studying: (1) whether pathological gamblers exhibit lower risk aversion than healthy controls (reflected in the curvature of the value function), (2) whether we could to replicate the finding of Ligneul and colleagues (2013) on general shift in risk preferences of pathological gamblers, (3) whether there are similar results in the loss domain, which was not included in the previous study, and (4) whether a dopaminergic manipulation has an effect on risk aversion (curvature of the value function), optimism about risk (elevation of the probability weighting function) and sensitivity to probabilities (distortion of the probability weighting function). Finally, we were also interested in looking into the potential relationship between dopamine synthesis capacity and prospect theory parameters as well as the effects of the dopaminergic manipulation on these parameters, due to potential effects of individual dopamine baseline levels on reward- and punishment-related behaviour (Cools et al., 2009; van Holst et al., 2016).

2. Methods

To study the effects of dopamine on risk-taking behaviour in pathological gambling, a group of pathological gamblers as well as healthy controls were recruited and subjected to a dopaminergic manipulation during a gambling task measuring risk-taking attitudes within the prospect theory framework. The behavioural data in this study was collected by Guillaume Sescousse, Lieneke Janssen, and Mahur Hashemi at the Donders Centre for Cognitive Neuroimaging, Radboud University, Nijmegen, in the Netherlands. The study was approved by the local ethical committee, Commissie Mensgebonden Onderzoek, region Arnhem-Nijmegen.

2.1. Participants

The study included healthy control (n = 21) and pathological gambler (n = 16) participants. Originally, 22 control and 22 gambler participants took part in the study. One gambler participant was excluded due to a loss of data for one session. One control participant and four gamblers were excluded due to extreme behaviours violating core assumptions of prospect theory (see section 2.4 for more details). The participants were matched on age, net income in Euros per month, and verbal IQ (see Table 1).

Table 1

Descriptive Statistics and Comparison of Means for Background Variables

	Healthy controls			Pathological gamblers					
Variable	Range	*M*	*SD*	Range	*M*	*SD*	*t*	*df*	*p*
Age	18–52	32.1	11.4	21–50	36.2	8.69	−1.07	35	.29
Net income	0–3570	1690	1123	750–3250	1779	927	−0.17	35	.87
Verbal IQ	85–128	106	9.47	77–123	103	12.3	0.80	35	.43

Note. M = Mean. SD = Standard Deviation. Statistical significance at the .05 level.

Participants were all men because pathological gambling is much more common in men (Welte, Barnes, Wieczorek, Tidwell, & Parker, 2001; also see Potenza et al., 2001 for gender differences in PG). Pathological gamblers were included based on an in-depth structured interview using *DSM-IV* criteria (American Psychological Association, 2000), with at least 5 criteria for PG present, and a South Oaks Gambling Screen (Lesieur & Blume, 1987) score of at least 5. Exclusion criteria were the consumption of more than four alcoholic beverages daily, use of psychotropic medication, lifetime history of schizophrenia, bipolar disorder, attention deficit hyperactivity disorder, autism, eating disorder, anxiety disorder, or obsessive compulsive disorder, and past six months history of major depressive episode. Gamblers with past and current cannabis dependence, lifetime history of dysthymia, and remitted post-traumatic stress disorder were included due to the high level of co-morbidity of PG with other psychiatric disorders (Lorains et al., 2011). All participants provided written informed consent in line with the declaration of Helsinki. The present task was part of a larger study for which the participants were paid €50 on each session. The other tasks in the study were a reversal learning task (Janssen et al., 2015), a slot machine task measuring sensitivity to near-misses (Sescousse et al., 2016a), and a mixed gamble task measuring loss aversion (Sescousse et al., 2016b).

2.2. Drug manipulation

Dopamine D_2/D_3 receptor antagonist sulpiride and a placebo drug were administered to the participants before the experiment on two separate days in a within-subjects design. The drug administration was double-blind and counterbalanced. Sulpiride, a highly selective antagonist for dopamine D_2/D_3 receptors (Vallone, Picetti, & Borrelli, 2000), was administered in a 400 mg (medium) dose. Sulpiride was chosen as the dopamine-modulating drug in this study based on a few reasons. First of all, D_2 agonists are known to cause pathological gambling symptoms in a subset of Parkinson's disease patients. Moreover, D_2/D_3 agents have been previously shown to modulate reward (here, gains) and punishment (losses) learning in human studies (Pizzagalli et al., 2008; Cools et al., 2009).

2.3. Task and data collection

The experiment described here was one out of four experiments in the same session, two of which were conducted in the fMRI scanner. The task is based on the "bisection method" elaborated by Abdellaoui and colleagues (2008, 2011). Participants made a series of decisions between a gamble and a sure option of winning a certain amount of money. The goal of each series of decisions in this iterative method is to reach an indifference point of the participant with regard to the sure option and the gamble (hence, the term "bisection"), that is, where the value of the sure option leads to maximal hesitation with the gamble. This is also called the *certainty equivalent*, reflecting the subjective value of the gamble. Each series of decisions had one type of gamble out of 10 different gambles, as shown in Table 2. Six of these gambles had variable amounts of money but the same probability of winning or losing, namely, 2/6. The other four gambles had variable probabilities of winning or losing, namely, 1/6, 3/6, 4/6, and 5/6, but the same amounts of money at stake.

Table 2

Gambles With Varying Outcomes and Probabilities

	Gamble									
Variable	1	2	3	4	5	6	7	8	9	10
x	1200	1200	600	1200	600	1000	1200	1200	1200	1200
p	1/6	2/6	2/6	2/6	2/6	2/6	2/6	3/6	4/6	5/6
y	0	0	0	600	300	400	900	0	0	0

Note. *x* is the larger amount of money in the gamble that could be won or lost with probability *p*. *y* is the smaller amount of money in the gamble that could be won or lost with probability 1−*p*. *x* and *y* are in €. For losses, the amounts of money were the same but negative.

The task is shown in Figure 3. Each series of decisions consisted of six trials, followed by two trials checking the consistency of the participant's choices. The starting amount of money in the sure option was fixed for each series and always corresponded to the expected value of the gamble. In the gamble, there was a chance of winning a certain amount of money with probability *p* or another amount of

money with probability 1−*p*. The choice for each trial was self-paced, after which the participant received feedback on their selection (a blue frame around the chosen option) for 500 ms, followed by 500 ms of fixation on a cross in the middle of the screen. The participant did not receive any information on the outcome of the trial, that is, which amount of money they won if they chose the gamble.

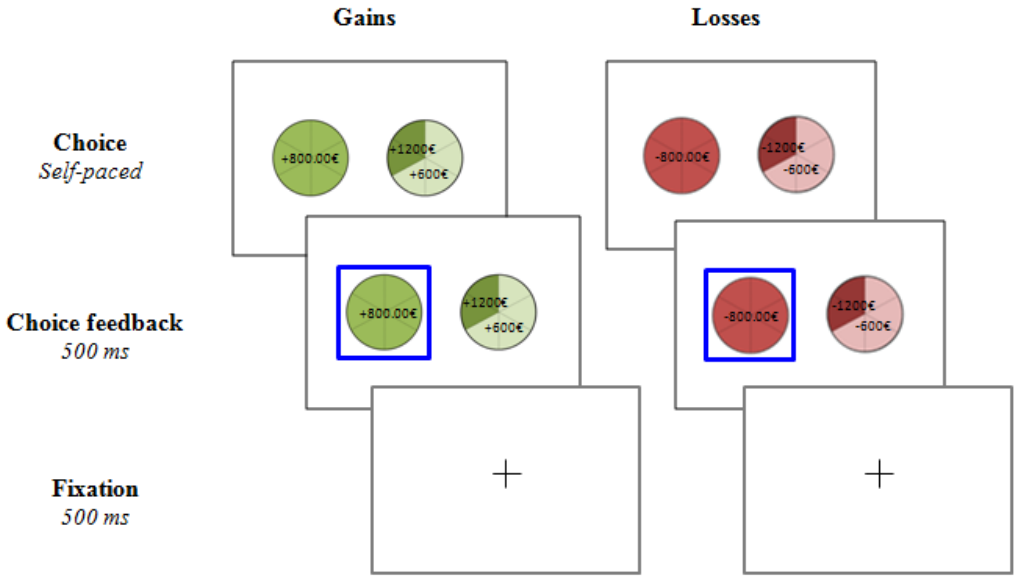

Figure 3. The gambling task. Each trial consisted of a self-paced choice, followed by 500 ms of feedback and 500 ms of fixation. The sure amount of the next trial was adjusted based on the choice, with the gamble being fixed for the series.

The iterative procedure was as follows. If the participant chose the sure option, the amount of money offered in the sure option was decreased on the next trial to increase the attractiveness of the gamble. If, on the other hand, the participant chose the gamble, the amount of money offered in the sure option was increased. After six trials, the participant had to go through a "consistency check" that ensured that their choice behaviour was consistent (and not random). After passing the check, the participant moved on to the next gamble and a new series of decisions. If the participant failed the check, they had to repeat the whole series of decisions until they passed the consistency check. The consistency check was included in order to ensure non-random choice behaviour and understanding of the task. In total, participants went through at least 80 experimental trials, consisting of six choice trials and two

consistency trials per series, with 10 different series. There could also be more trials if the participant failed the consistency check and had to repeat the series. The order of gambles was randomized.

The task was exactly the same in the loss domain but with negative amounts of money. Gain and loss trials were presented in separate blocks and the order of the blocks was counter-balanced across participants and drug sessions. Before the actual experiment, participants had three training series, two for gains and one for losses. The task presentation was created with the Psychophysics Toolbox (version 2) for MATLAB (Brainard, 1997; Kleiner, Brainard, & Pelli, 2007; Pelli, 1997).

2.4. Estimation procedure

The estimation procedure in this study is based on the semi-parametric method used by Abdellaoui, Diecidue and Öncüler (2011) and earlier described in Abdellaoui, Bleichrodt and L'Haridon (2008). Abdellaoui and colleagues consider this method an improvement over other methods due to its efficiency in measuring subjective utility as well as due to the relatively small cognitive burden on the subjects. In the semi-parametric method, the parameters of value function and probability weighting function are retrieved in a sequential two-step estimation procedure. The estimation procedure was conducted separately for gains and losses and for the drug and placebo conditions, within each individual participant. In the first step of the estimation, certainty equivalents of gambles 2 to 7 in Table 2, with varying amounts of money but the same probability of 2/6, were used to estimate the curvature parameter of the value function (also called α) as well as the probability weight of 2/6 (also called $w(2/6)$) in a parametric manner. Non-linear least squares estimation was applied to find the values that best fit the data, that is, the certainty equivalents, by minimizing a sum of squares function. We used a function from Abdellaoui et al. (2011) to fit on the certainty equivalent data, including two free parameters, one for the curvature parameter of the value function and one for the weight of probability 2/6, which could be estimated based on the varied outcome values in the gambles with this probability (Table 1, gambles 2–7).

According to the prospect theory, a certainty equivalent of a binary gamble (with only gains or losses) is given by the subjective utility of the outcome weighted by its probability, in this case:

$$U(CE) = w(p)U(x) + \big(1 - w(p)\big)U(y) \tag{1}$$

CE is a certainty equivalent, while *x* is the amount of money to be won with probability *p* and *y* the amount of money to be won with probability 1−*p*. This can also be expressed as:

$$U(CE) = w(p)(U(x) - U(y)) + U(y) \tag{2}$$

Then, the utilities can be replaced with the value function form x^{α}:

$$CE^{\alpha} = w(p)(x^{\alpha} - y^{\alpha}) + y^{\alpha} \tag{3}$$

Finally, we can shift out the power on the certainty equivalent and get:

$$CE = [w(p)(x^{\alpha} - y^{\alpha}) + y^{\alpha}]^{\frac{1}{\alpha}} \tag{4}$$

The certainty equivalents are known from the data. The value of α parameter was initialised as a common value from literature, 0.88 (see Fox & Poldrack, 2008) and *w*(2/6) was initialised as .33 to match the probability 2/6 of the gamble data used to in this estimation step. Therefore, we get the following function to be optimised in order to get values for α parameter and the subjective weight of probability 2/6:

$$\widehat{CE}(i) = [w(2/6)((x_i)^{\alpha} - (y_i)^{\alpha}) + (y_i)^{\alpha}]^{\frac{1}{\alpha}} \tag{5}$$

$\widehat{CE}(i)$ is the estimate of the certainty equivalent of gamble i = 2, 3, … , 7. This is the exact form used in Abdellaoui et al. (2011). Next, the probability weights for the rest of the probabilities were calculated based on the certainty equivalents from gambles 1 and 8–10 in Table 2 and the individual α parameters,

with p = 1/6, 3/6, 4/6, 5/6. To calculate the probability weights, we can take the part of the Equation 3 related to outcome *x* with probability *p*:

$$CE = w(p)x^{\alpha} \tag{7}$$

Then, we get the form of the equation for the non-parametric estimation of the probability weights based on the certainty equivalents, values *x* from the gambles, and the estimated α parameter:

$$w(p) = \frac{CE^{\alpha}}{x^{\alpha}} \tag{8}$$

In the second step of the estimation procedure, *w*(2/6) and *w*(*p*) for probabilities 1/6, 3/6, 4/6, and 5/6 were used for the parametric estimation of the elevation and distortion parameters (also called δ and γ) of the probability weighting function, relating to the general optimism about risk and sensitivity to probabilities. The values of δ and γ parameters were initialised as common values from literature: 0.8 and 0.6 (see Fox & Poldrack, 2008). Non-linear least squares estimation was applied on the Lattimore function (Lattimore et al., 1992), optimising the fit with the probability weights:

$$w(p) = \frac{\delta p^{\gamma}}{\delta p^{\gamma} + (1-p)^{\gamma}} \tag{9}$$

One control participant and four gamblers were excluded from the estimation procedure. Statistical analysis included the participants that passed the following criterion: the weight of probability 1/6 should not be higher than the weight of probability 5/6. That is, participants who exhibited behaviour where the first probability weight was higher than the last one were excluded because their behaviour in the task violates the basic assumption of monotonicity in the evaluation of probabilities. One gambler participant was excluded due to highly controlled and extremely risk averse behaviour (α value over three standard deviations away from the mean).

2.5. Statistical analysis

In the statistical analysis, α, δ, and γ parameters of prospect theory were compared across groups and drug conditions with non-parametric statistics due to the non-normal distribution and small sample size of the data. In the case of independent samples (comparing groups), Mann-Whitney *U* tests were used. The distributions of α, δ, and γ parameters for the two groups have different shapes and, therefore, in the case of Mann-Whitney *U* tests, mean ranks are reported instead of medians were reported as a measure of central tendency. In the case of related samples (comparing drug conditions), Wilcoxon signed-rank tests were used and medians were reported as a measure of central tendency. To assess the robustness of the results with parametric tests, the prospect theory parameter values were log-transformed. In a secondary analysis, the parameters were also correlated with baseline dopamine synthesis capacity measures obtained in an F-DOPA PET experiment (van Holst et al., 2016) in a subset of participants (pathological gamblers, $n = 9$; control subjects, $n = 16$). Only the prospect theory estimates measured in the placebo condition were correlated with the PET measures. The regions of interest were the ventral striatum and the putamen. Moreover, the drug effects associated with each of the parameters α, δ, and γ were also correlated with the same PET measures. The groups were analysed together due to the too small overlapping sample size of the gamblers for the prospect theory and F-DOPA measures ($N = 25$). Spearman correlation coefficients were used due to the non-normal distributions of the data. All analyses were conducted in SPSS.

3. Results

We expected that pathological gamblers would have lower risk aversion than the control participants, reflected in lower sensitivity to outcomes, that is, higher curvature value (less concavity in the gain domain, more convexity in the loss domain) of the value function. Moreover, based on the study by Ligneul and colleagues (2013), we expected pathological gamblers to have higher elevation of the probability weighting function compared with the control participants in the gain domain. We also expected pathological gamblers to have lower elevation than the control participants in the loss domain, reflecting more optimistic attitude toward probabilities and thus more risk-seeking. Finally, we expected to find an effect of the dopaminergic manipulation at least on the distortion of the probability weighting function based on the results of Takahashi and colleagues (2010). We also potentially expected that pathological gamblers would be differently affected by the dopaminergic manipulation compared with the control participants, based on the results of two other studies in the same protocol (Janssen et al., 2015; Sescousse et al., 2016b). In line with this, we expected that endogenous dopamine synthesis capacity measured with F-DOPA PET (van Holst et al., 2016) would correlate with some of the prospect theory parameters and/or the potential drug effect on these parameters. However, we did not have specific hypotheses on the direction of the drug effect because the literature on the effects of dopaminergic drugs on risk-taking remains scarce and does not provide enough support for making such hypotheses.

3.1. Risk aversion

We first examined a model-free measure, the proportion of risk averse participants (%), which was calculated based on the certainty equivalents (CEs). It was defined that if at least 7 out of 10 of the 10 CEs of a participant were smaller than the expected value (EV) of the associated gamble, they were risk averse (similar to the at least 2/3, or ~67%, criterion in Abdellaoui et al., 2011). Table 3 presents the numbers of risk averse participants. There was no difference in risk aversion between controls and gamblers in the placebo or sulpiride conditions, either in the gain domain, or in the loss domain.

Table 3

Numbers of Risk Averse Participants

	Placebo						Sulpiride					
	Controls		Gamblers		Test		Controls		Gamblers		Test	
Domain	No.	%	No.	%	$\chi^2(1)$	*p*	No.	%	No.	%	$\chi^2(1)$	*p*
Gains	12	57.1%	7	43.8%	0.65	.42	13	61.9%	5	31.3%	3.42	.065
Losses	12	57.1%	5	31.3%	2.45	.18	10	47.6%	7	43.8%	0.055	.82

Note. Controls $n = 21$, gamblers $n = 16$.

3.2. Sensitivity to outcomes

In our model-based approach, sensitivity to outcomes was reflected by the prospect theory parameter α. Table 4 reports the estimates of the parameters α, δ, and γ in the study. Tests on the α parameter indicated that there was no statistically significant difference between control participants (Mean rank = 17.7) and pathological gamblers (Mean rank = 20.6) in sensitivity to outcomes in the gain domain, $U = 196$, $p = .40$. There was also no significant difference between control participants (Mean rank = 17.2) and gamblers (Mean rank = 21.4) in the loss domain, $U = 206$, $p = .25$.

Table 4

The Estimates of Prospect Theory Parameters

	Placebo				Sulpiride			
	Controls		Gamblers		Controls		Gamblers	
Parameter	Median	IQR	Median	IQR	Median	IQR	Median	IQR
α_{gains}	0.74	0.66	0.80	0.37	0.80	0.42	1.16	0.81
α_{losses}	1.01	1.14	1.92	1.46	1.28	0.64	1.36	0.95
δ_{gains}	0.99	0.86	0.90	0.51	0.93	0.85	0.68	0.61
δ_{losses}	1.08	0.76	0.52	0.38	0.88	0.56	0.78	0.99
γ_{gains}	0.53	0.50	0.62	0.42	0.66	0.54	0.89	0.49
γ_{losses}	0.97	0.60	0.88	0.77	0.99	0.30	0.72	0.72

Note. IQR = Interquartile range.

Moreover, there was no effect of drug, that is, difference between the placebo (*Mdn* = 0.79) and sulpiride (*Mdn* = 0.93) conditions, in the gain domain, $W = 453$, $Z = 1.53$, $p = .13$. There also was no difference between placebo (*Mdn* = 1.52) and sulpiride (*Mdn* = 1.28) conditions in the loss domain, $W = 271$, $Z = -1.21$, $p = .23$. However, a test for a drug-by-group interaction indicated that the effect of the drug was significantly different between the controls (Mean rank = 15.9) and gamblers (Mean rank = 23.0) in the gain domain, $U = 233$, $p = .047$. According to a post hoc test, there was no difference in the placebo condition between pathological gamblers (Mean rank = 19.1) and control participants (Mean rank = 18.9), $U = 167$, $p = .99$. In the sulpiride condition, there was a trend-level difference between gamblers (Mean rank = 18.1) and controls (Mean rank = 22.9), with gamblers tending to be more risk-seeking than controls, $U = 230$, $p = .059$. Note that the significance level here is .025 (.05/2), corrected for two comparisons. In the loss domain, there was no significant drug-by-group interaction, $U = 113$, $p = .095$.

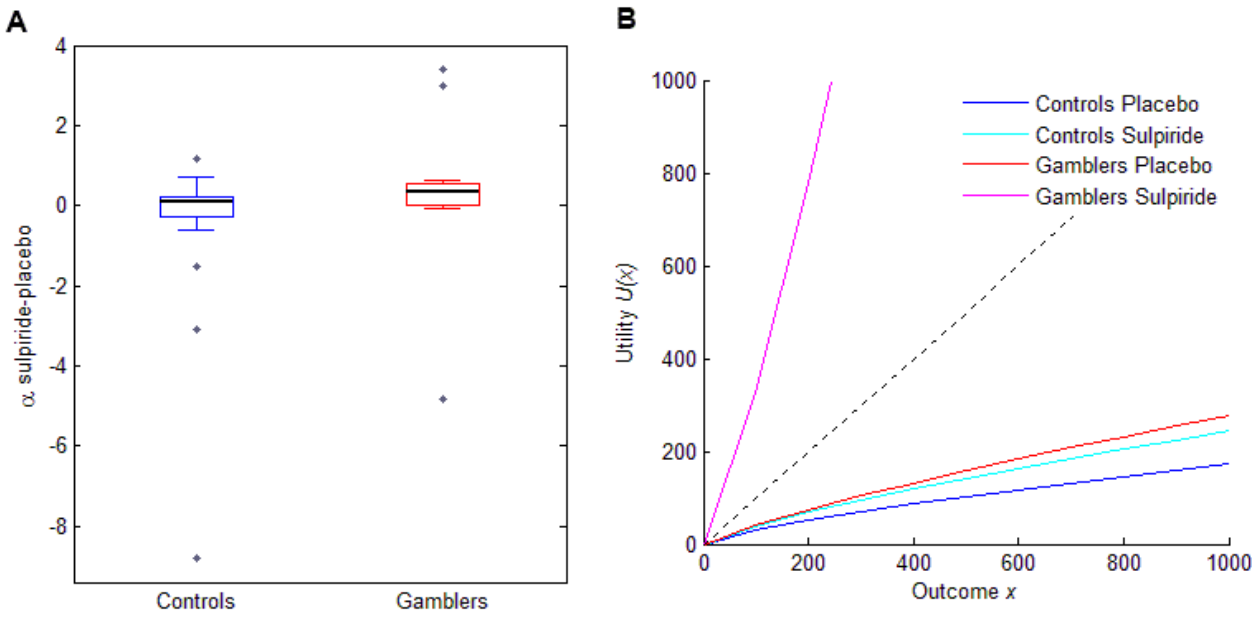

Figure 4. *A*. The effect of drug (sulpiride−placebo) on the curvature parameter α across groups in the gain domain, *B*. The fitted value function. The used values of α are medians of each group and condition.

3.3. Optimism about risk

A change in the elevation parameter δ of the probability weighting function represents a shift in the weighting of the entire probability range, thus reflecting overall optimism or pessimism about risk. The medians and IQR of δ can be seen in Table 4. There was no statistically significant difference between control participants (Mean rank = 21.2) and pathological gamblers (Mean rank = 16.1) in optimism about risk in the gain domain, $U = 122$, $p = .17$. However, there was a significant difference between control participants (Mean rank = 22.2) and gamblers (Mean rank = 14.8) in optimism about risk in the loss domain, $U = 100$, $p = .037$. Gamblers had lower δ parameter, indicating lower elevation of the probability weighting function in the loss domain, making the gambler participants more risk-seeking compared with control participants.

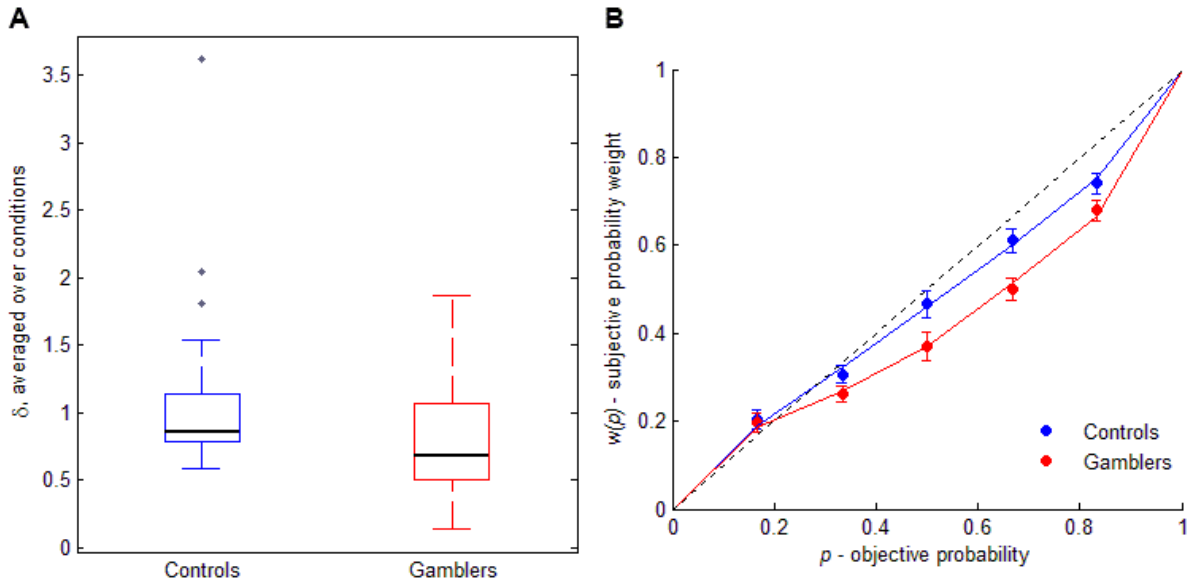

Figure 5. *A.* Group effect (average of placebo and sulpiride conditions) on the elevation parameter δ in the loss domain, *B.* Fitted probability weighting function and the five probability weight data points. Lower elevation reflects more risk-seeking for losses. The error bars are standard error of the mean (SEM).

Moreover, there was no effect of drug, that is, no significant difference between the placebo (*Mdn* = 0.97) and sulpiride (*Mdn* = 0.79) conditions in the gain domain, $W = 321$, $Z = -0.46$, $p = .65$. There also was no difference between placebo (*Mdn* = 0.72) and sulpiride (*Mdn* = 0.80) conditions in the loss

domain, $W = 356$, $Z = 0.068$, $p = .95$. Furthermore, the effect of the drug was not significantly different between the controls (Mean rank = 20.1) and gamblers (Mean rank = 17.6) in the gain domain, $U = 233$, $p = .50$. There was also no difference between the effect of the drug for controls (Mean rank = 16.7) and gamblers (Mean rank = 22.1) in the loss domain, $U = 218$, $Z = 1.53$, $p = .13$.

3.4. Sensitivity to probabilities

The level of distortion, or nonlinearity, in the subjective sensitivity to probabilities is reflected in the parameter γ. The median and IQR estimates can be found in Table 4. A test on the γ parameter showed no statistically significant difference between control participants (Mean rank = 17.0) and pathological gamblers (Mean rank = 21.7) in sensitivity to probabilities in the gain domain, $U = 211$, $p = .20$. There was also no significant difference between control participants (Mean rank = 20.9) and gamblers (Mean rank = 16.6) in sensitivity to probabilities in the loss domain, $U = 129$, $p = .24$.

However, there was a significant effect of the drug, that is, a difference between the placebo (*Mdn* = 0.53) and sulpiride (*Mdn* = 0.69) conditions in the gain domain, $W = 555$, $Z = 3.1$, $p = .002$. Participants had higher values of the γ parameter in the gain domain, indicating lower levels of distortion of the probability weighting function, and therefore, less overweighting of low probabilities and underweighting of moderate to high probabilities. Post hoc test showed that there was no significant difference between placebo (*Mdn* = 0.53) and sulpiride (*Mdn* = 0.66) conditions for control participants, $W = 161$, $Z = 1.58$, $p = .11$. However, there was a significant difference between placebo (*Mdn* = 0.62) and sulpiride (*Mdn* = 0.89) for the pathological gamblers, $W = 120$, $Z = 2.69$, $p = .007$, showing that gamblers had higher γ parameter and therefore lower distortion of the probability weighting function in the sulpiride condition compared with the placebo condition. The result survives a Bonferroni correction for multiple comparisons with significant p at .025 (.05/2). In the loss domain, there was no difference between placebo (*Mdn* = 0.97) and sulpiride (*Mdn* = 0.96) conditions overall, $W = 359$, $Z = 0.11$, $p = .91$.

Moreover, the effect of drug was not significantly different between the control group (Mean rank = 17.8) and gambler group (Mean rank = 20.9) in the gain domain, U = 198, p = .37. The difference between controls (Mean rank = 21.8) and controls (Mean rank = 15.4) was at trend level in the loss domain, U = 110, p = .078.

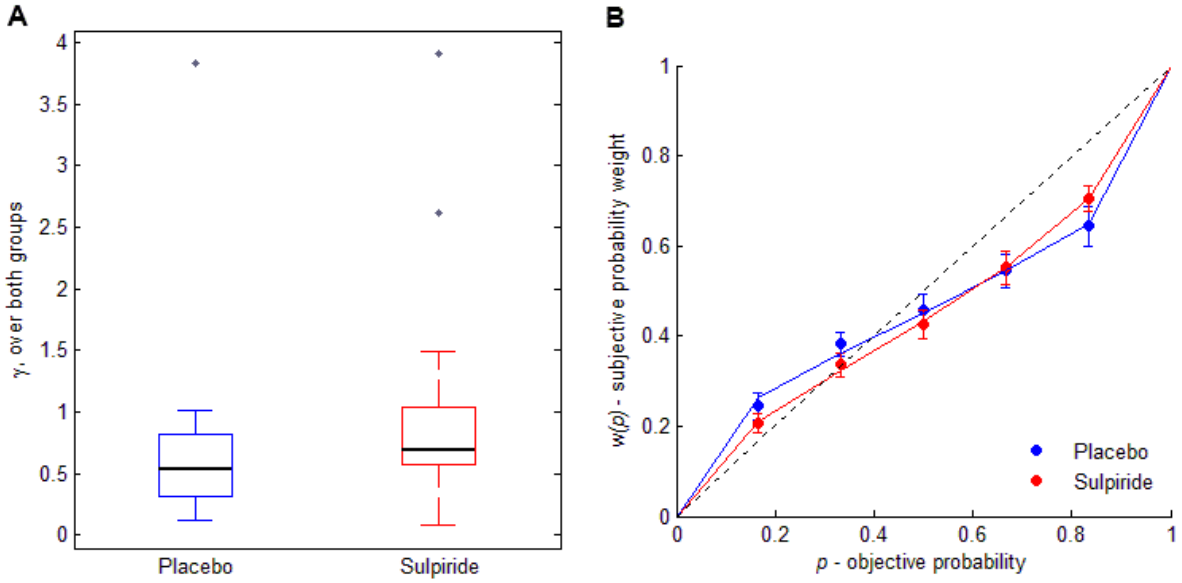

Figure 6. A. Drug effect (sulpiride−placebo) on the distortion parameter γ in the gain domain, *B.* Fitted probability weighting function and the five probability weight data points. Higher values of γ reflect lower level of distortion in the probability weighting function. The error bars are SEM.

3.5. Endogenous dopamine levels

There were no significant correlations between any of the prospect theory parameter values or their associated drug effects and the F-DOPA PET measures on dopamine synthesis capacity, either in the ventral striatum or the putamen. However, all of the non-significant results are reported in Table 5 in the interest of interpretation and potential meta-analyses.

Table 5

Results of the Correlations Between Dopamine Synthesis Capacity and Prospect Theory Parameters

	Gains				Losses			
	Ventral striatum		Putamen		Ventral striatum		Putamen	
Parameter	r_s	p	r_s	p	r_s	p	r_s	p
α	.031	.85	.082	.70	−.062	.77	.015	.94
α_{drug}	−.12	.57	−.085	.69	.057	.79	−.001	.997
δ	.22	.30	−.20	.33	.030	.89	−.067	.75
δ_{drug}	−.005	.98	.004	.99	−.015	.95	.00	1.0
γ	.029	.89	.17	.43	−.19	.37	−.10	.63
γ_{drug}	−.15	.48	−.22	.29	−.045	.83	−.16	.46

Note. $N = 25$. r_s is the correlation coefficient of a Spearman correlation. Drug effect is sulpiride−placebo.

3.6. Sensitivity analyses

The results obtained with non-parametric statistics were replicated with parametric statistics, with some exceptions. The α parameter drug by group interaction in the gain domain was not significant at .05 level in parametric analysis of variance (ANOVA) with log-transformed values, $F(1, 35) = 3.14$, $p = .085$, $\eta^2 = .082$. The group effect on δ in the loss domain was replicated with parametric ANOVA, $F(1, 35) = 5.53$, $p = .024$, $\eta^2 = .14$, as was the drug effect on γ in the gain domain, $F(1, 35) = 9.85$, $p = .003$, $\eta^2 = .22$.

To explore robustness of the results on probability weighting, parametric repeated-measures ANOVAs were conducted on the (model-free) values of probability weights. As expected based on the non-parametric results of the estimated δ parameter, the probability weights did not differ between the groups in the gain domain, $F(1, 35) = 0.14$, $p = .71$, $\eta^2 = .004$. In addition, there was a significant difference in the probability weights between the groups in the loss domain, $F(1, 35) = 4.52$, $p = .041$, $\eta^2 = .11$, in accordance with the group difference on the elevation of the probability weighting function. To further explore robustness of the results based on model-free data, parametric repeated-measures ANOVAs were conducted on the certainty equivalents. There were no significant effects of group or drug on the certainty equivalents.

Furthermore, it was confirmed that the results remained unchanged when Prelec two-parameter function (Prelec, 1998) was used, instead of the Lattimore function (Lattimore et al., 1992), to estimate the δ and γ parameters. The Prelec function has a different form compared with the Lattimore function:

$$w(p) = e^{-\delta(-\ln p)^{\gamma}} \tag{7}$$

There was no qualitative change in the results when the same analyses were conducted on the parameter values obtained with the Prelec function as were conducted on those obtained with the Lattimore function. The results also stayed qualitatively similar when α parameter was not estimated but was assumed to be 1, making the value function linear like in the study by Ligneul and colleagues (2013). When all possible participants were included, with no control participants (n = 22) or pathological gamblers (n = 21) excluded due to the behavioural criteria, the results were qualitatively similar as well.

Moreover, parameters were successfully recovered from simulated data generated from estimated parameters. The parameter values from the original estimation procedure were used in calculating new certainty equivalents with Equation 5, except for $w(2/6)$ being replaced with more general form $w(p)$:

$$CE(i) = [w(p_i)((x_i)^{\alpha} - (y_i)^{\alpha}) + (y_i)^{\alpha}]^{\frac{1}{\alpha}} \tag{8}$$

p = 1/6, 2/6, 3/6, 4/6, 5/6 is the probability of the outcome x, with y being the alternative outcome with probability $1-p$. These new simulated data were then used to calculate new $w(p)$, which were used as input in the original two-step procedure in order to estimate α, δ, and γ parameters again. The correlations between the original and the recovered parameter values were all above r = .95, with p < .001, in both the gain and loss domain.

The chance that the original literature-based starting values and the single iteration estimation procedure would lead to a local but not global minimum was explored with an iterative approach with randomized starting values. The procedure was run with different numbers of iterations (e.g., 40, 80, 200) and the starting values were randomly drawn from [0, 5] for parameters α, δ, and γ, and from [0, 1] for

w(2/6). The squared two-norm of the residual ('resnorm') reflecting the goodness-of-fit between the model output and the data was used to select the smallest previous value at each iteration so that, in the end, the prospect theory parameter values with the smallest resnorm were retained. These parameter values were compared with the original values obtained with the non-iterative estimation procedure with literature-based starting values. The original and resnorm-based parameter values (α, δ, and γ) were perfectly correlated for both gains and losses as well as both groups and drug conditions (r_S = 1.0, p < .001). For example, with 40 iterations, the resulting parameter values were always less than 0.01 and on average around 0.0001 units away from the original values. Consequently, it seems safe to say that the original parameter values were obtained based on a global, not local, minimum and that the estimation procedure is stable.

Finally, there exists a well-known identifiability issue in prospect theory with regard to α and δ parameters (e.g., Fox & Poldrack, 2008). In this study, α and δ were negatively correlated, showing that there might indeed be an identifiability issue also in this study. The two parameters showed a strong negative relationship ($r_S \leq -.58$, $p \leq .006$) for both gains and losses and both groups and conditions, except for gambler participants in the placebo condition in the gain domain, $r_S(14) = -.49$, $p = .052$ and in the loss domain, $r_S(14) = -.30$, $p = .26$. Therefore, the results on α and δ parameters might not be reliable and should be interpreted cautiously, although it is also worth mentioning that the two parameters were estimated in different steps and based on different data. Namely, α was first estimated based on the certainty equivalents derived from gambles with a fixed probability, after which δ was estimated from the probability weights and certainty equivalents derived from gambles with fixed amounts in a separate step.

4. Discussion

This study investigated the effects of dopaminergic modulation on risk-taking behaviour in pathological gamblers and healthy participants with a prospect theory approach. We found that modulating dopamine through D_2/D_3 receptor antagonism decreased probability distortion, making participants more rational in their subjective assessment of probabilities in the gain domain. This result was replicated with parametric statistics and a model-free analysis of probability weights. However, we did not find evidence for differences in sensitivity to outcomes between pathological gamblers and healthy control participants as well as no effect of the drug on sensitivity to outcomes. Moreover, we did not find evidence for a difference between pathological gamblers and healthy controls in optimism about risk, as captured by the elevation of probability weights, in the gain domain. We did find such a difference in the loss domain though, where pathological gamblers were more optimistic about risk compared with the control participants. Finally, we did not find evidence for a relationship between dopamine synthesis capacity and any of the prospect theory parameters or their associated drug effects.

4.1. Dopamine and distortion of probability weighting

As far as we know, this study is the first one to investigate the effects of dopaminergic modulation on risk-taking behaviour in both pathological gamblers and healthy participants, within the prospect theory framework. It has been speculated before that striatal dopamine transmission might be involved in probability weighting (Trepel, Fox, & Poldrack, 2005). Accordingly, there is indirect evidence from an fMRI study showing a link between the non-linearity of probability weighting function and activity in the ventral striatum (Hsu, Krajbich, Zhao, & Camerer, 2009). We found that probability weighting, more specifically the distortion or non-linearity of the probability weighting function, is modulated by dopamine D_2/D_3 receptor antagonism. The result appears robust based on several different sensitivity analyses. Similarly, Takahashi et al. (2010) found a relationship between dopamine function and probability weighting. In their PET study, lower dopamine D_1, but not D_2, receptor binding capacity in the

striatum was associated with higher levels of distortion in probability weighting. However, based on our findings, it seems that D_2 (and D_3) receptors are linked to probability weighting as well. Therefore, our study shows that a neurobiological mechanism, specific D_2/D_3 antagonism, can be linked to a particular behavioural component of decision-making under risk, distortion of probably weighting.

The drug effect observed in the current study could reflect a change in the balance of D_1 and D_2 receptor signalling with sulpiride-induced D_2/D_3 receptor blockade leading to increased post-synaptic D_1 receptor stimulation (see van der Schaaf et al., 2014). Accordingly, we observed that specific D_2/D_3 receptor blockage with sulpiride decreases distortion, which fits together with the Takahashi et al. finding on higher D_1 receptor binding capacity in the striatum being associated with less distortion. Interestingly, despite not finding a drug-by-group interaction in our data, a post hoc test suggested that the drug effect on the distortion of probability weighting was mainly driven by pathological gamblers in our study. A potential explanation for the lack of D_2 receptor-related results in the Takahashi et al. study is that they only included healthy controls. In the current study, healthy controls did not exhibit significantly different levels of distortion under sulpiride compared with the placebo condition. Finally, Takahashi et al. used a probability weighting function with only one parameter. It could be that some of the variance in their study could also be explained by the elevation parameter that was not estimated, even though we did not find robust evidence for the dopaminergic modulation of the elevation parameter in our study.

Rutledge and colleagues (2015) modulated dopamine with L-DOPA in healthy participants who played a gambling task almost identical to the one used in this study. They found a robust effect of the drug on raw behavioural measures while there were no evident changes found in the current study. One reason for this could be that Rutledge et al. provided feedback to their participants after each trial, which was not included in this study on purpose to avoid the effect of outcomes on consequent trials. There is a difference between decisions from description, like in the current study, and from experience, such as when there is learning based on previous outcomes (Hertwig & Erev, 2009). Moreover, Rutledge et al. concluded that a prospect theory decision model could not explain their behavioural observation of L-DOPA increasing the number of gambles chosen in gain trials. Instead, a Pavlovian approach-avoidance

model provided a better fit. While Rutledge and colleagues used a slightly different modelling approach, it seems that the results related to outcome sensitivity and risk aversion are consistent in the two studies. Based on the findings of Rutledge et al., it could be that the prospect theory framework is not optimal to reveal the effects of dopaminergic manipulation on risk-taking behaviour. The iterative procedure implemented in the experimental design of the current study was optimised for the certainty equivalent approach. Therefore, it does not allow us to apply the approach bias softmax model of Rutledge et al. to our data and make direct comparisons. Furthermore, Rutledge et al. did not estimate the probability weighting function and therefore we do not know whether L-DOPA would induce similar drug response on probability weighting as was observed in the current study. Finally, it is difficult to compare the neurobiological effects of a general 'boost' in dopamine caused by L-DOPA, a metabolic precursor of dopamine, and specific D_2/D_3 receptor antagonism in behavioural studies.

4.2. Risk attitudes and pathological gambling

We did not find evidence in support of the central result of Ligneul and colleagues (2013) that showed a global shift in optimism about risk in pathological gamblers in the gain domain. An interesting point of difference between the current study and the Ligneul et al. study is that much higher amounts of money were used in the gambling task in this study. It has been observed that higher amounts of money lead to more risk aversion for gains, whereas people tend to be risk-seeking for small-stake gains (and the opposite for losses), called the "peanuts effect" (Prelec & Loewenstein, 1991; see also Weber & Chapman, 2005). In the Ligneul et al. study, the gamblers might not have cared as much for the lower amounts of money at stake, therefore being more risk-seeking than the gambler participants in the current study. This could have made our groups more similar with regard to their risk attitudes. It could also be that the control participants in this study happened to be more risk-seeking than usually, which could have affected the fact that we could not find differences in outcome sensitivity and risk aversion between the controls and pathological gamblers. However, we do see an expected direction in the number of risk

averse participants, with more risk-seeking participants among gamblers than controls. Abdellaoui et al. (2011) report that 77% of their subjects (N = 52) exhibited risk aversion under a criterion only slightly more relaxed than ours (8/12 certainty equivalents smaller than the expected values of gambles, versus our 7/10). However, out of our healthy control participants in the placebo condition, only around 57% were risk averse. On the other hand, the model-based approach does not give support to this idea. The median curvature parameter of the value function for control participants in the placebo condition in the gain domain was 0.74 in the current study and 0.86 in the Abdellaoui et al. study, suggesting that the participants in the Abdellaoui et al. study were not less sensitive to outcomes, reflecting risk aversion, than the comparable participants in the current study.

Ligneul et al. assumed the value function to be linear ($\alpha = 1$) and did not estimate it from the data, while in this study, the value function was estimated based on the certainty equivalents. As was mentioned earlier, there is a known issue of identifiability, or a trade-off, between the curvature (α) and elevation (δ) parameters of prospect theory. Therefore, it could be that part of the risk-seeking behaviour was absorbed by the α parameter in the modelling procedure of the current study, whereas all of it was absorbed by the δ parameter in the study of Ligneul and colleagues. However, as mentioned in the methods section, the estimation procedure was also run with the linear value function and our results remained qualitatively unchanged. Interestingly, we did find a result similar to the main result of Ligneul et al. in the loss domain, which was not included in their study. Nevertheless, in accordance with the identifiability issue, an anti-correlation was observed between the two parameters in this study. Therefore, we are not confident in making distinct conclusions about the α and δ parameter results.

4.3. Dopamine synthesis capacity, drug response, and risk-taking behaviour

Van Holst and colleagues (2016) found that pathological gamblers and healthy controls have different levels of dopamine synthesis capacity as measured with F-DOPA PET, affecting their endogenous dopamine levels and thus possibly the effects of any dopaminergic drugs on their behaviour,

as has been seen before in healthy participants (Cools et al., 2009). Consequently, it would be reasonable to expect pathological gamblers and healthy controls to have different responses to dopaminergic drugs. However, we did not find any group differences in the observed drug effect in this study. Moreover, we explored the potential relationship between individual levels of dopamine synthesis capacity and risk-taking behaviour as modelled by the prospect theory parameters. Even though the groups of this study were pooled for more power, the correlations showed extremely low effect sizes, and therefore it is unlikely that any underlying robust relationship exists between the prospect theory parameters and dopamine synthesis capacity in the ventral striatum and the putamen.

On the other hand, pathological gamblers are a heterogeneous group and many studies have found that there are different subtypes of PG, for example, impulsive and emotional gamblers (e.g., Blaszczynski & Nower, 2002). It could be that these different types of gamblers had different responses to the drug in our study, making the drug response of the overall PG group indistinguishable from the drug response of the healthy control group. There is indeed evidence for different responses of high- and low-impulsivity gamblers to a dopamine-increasing stimulant drug (Zack & Poulos, 2009), suggesting that different types of gamblers could have different responses to dopaminergic drugs in general and perhaps even differences in baseline levels of dopamine. Unfortunately, the small overlapping number of gamblers who had both the PET and prospect theory measures made it infeasible to test this idea in our data.

4.4. Caveats of the study

One methodological weakness might be that there was only one probability point below 1/3. It would be better to have denser sampling of probability points for more reliable estimation of the probability weighting function, especially in order to reliably capture the overweighting of low probabilities. Another potential caveat is that there is evidence for poor retest reliability with regard to behavioural decision-making measures in addictive disorders such as pathological gambling (Kräplin, Scherbaum, Bühringer, & Goschke, 2016). This could mean that differences in decision-making behaviour

found with current tasks are not reliable indicators of actual group differences. Moreover, it could be that the current sample has an under- or overrepresentation of certain type of gamblers, which would make it non-representative of PG in general, especially as all of the participants in this study were male and emotional gambling has been more strongly associated with female gamblers (Ledgerwood & Petry, 2006). These different subtypes cannot be easily distinguished with the data that is available in this study. However, the study includes psychometric measures such as impulsivity, which is a psychological trait delineating these different types of gamblers. We explored the possibility that non-planning impulsivity (sub-scale of BIS11) score would be associated with differences in the prospect theory parameters, specifically the sensitivity to probabilities, but found no supporting evidence for this.

4.5. Conclusions

In summary, this study provides supporting evidence for the hypothesis that modulating dopamine can affect how humans weight probabilities during decision-making. Dopamine D_2/D_3 receptor antagonism shifts biases in the weighting of probabilities in the direction of more objective, economically rational decision-making. Moreover, it would be interesting to compare the contributions of D_1 and D_2/D_3 receptors with the same method since the effect has now been observed in relation to both of these receptors. In the future, more studies are needed to investigate the specific role of dopamine in risk-taking in healthy individuals as well as in pathological gamblers and other psychiatric populations. It would be of high clinical relevance to explore the different responses of healthy individuals and individuals suffering from pathological risk-taking to dopaminergic medication, as well as the potential influence of individual endogenous dopamine levels on these drug responses.

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